

Support for claims 25 - 40 can be found throughout the specification, and particularly as follows.

The conjugation of steroids to neurotrophins and neurotrophin fragments is disclosed, *inter alia*, at page 4, line 26 - page 5, line 5; page 7, lines 9 - 12; page 10, line 23 - page 11, line 2; page 14, lines 20 - 24; and Table 3, page 27.

4-pregnen and 1,4-pregnadiene steroids are specifically disclosed throughout the specification, and in particular as follows:

cortisone (4-pregnen-17 $\alpha$ , 21-diol-3,11,20-trione) at page 5, line 5; page 11, line 2; and page 20, line 12;

betamethasone (1,4-pregnadien-9 $\alpha$ -fluoro-11 $\beta$ , 17 $\alpha$ , 21-triol-16 $\beta$  methyl-3,20-dione) in Table 3, page 27;

dexamethasone (1,4-pregnadien-9 $\alpha$ -fluoro-11 $\beta$ , 17 $\alpha$ , 21-triol-16 $\alpha$  methyl-3,20-dione) in Table 3, page 27;

triamcinolone acetonide (1,4-pregnadien-9 $\alpha$ -fluoro-11 $\beta$ , 16 $\alpha$ , 17 $\alpha$ , 21-tetrol 3,20-dione 16,17-acetonide) in Table 3, page 27;

fluocinolone acetonide ({(6 $\alpha$ , 11 $\beta$ , 16 $\alpha$ )- 1,4-pregnadiene-6,9-difluoro-11,21-dihydroxy-16,17[(1-methylethylidene)bis(oxy)]- 3,20-dione, cyclic 16,17 acetal with acetone} in Table 3, page 27; and

corticosteroids (which include, *inter alia*, cortisol (4-pregnen-11,17,21-triol-3,20-dione), cortisone (4-pregnen-17,21-diol-3,11,20-trione), deoxycorticosterone (4-pregnen-21-hydroxy-3,20-dione), prednisone (1,4-pregnadien-17 $\alpha$ ,21-diol--3,11,20-trione), prednisolone (1,4-pregnadiene-11 $\beta$ ,17 $\alpha$ ,21-triol-3,20-dione), beclomethasone (1,4-pregnadiene-9-chloro-11 $\beta$ ,17,21-triol-16 $\beta$ -methyl-3,20-dione-17,21-dipropionate)) generically at page 14, line 20).

Carbamate linkages are disclosed in the hydroxyl group conjugation reaction shown in Table 4: hydroxyl attack of the PMPI isocyanate group yields a carbamate linkage.

Phosphoramidate linkage is shown in Table 4.

Linkage of the neurotrophin receptor via epsilon amino groups of its lysine residues is disclosed, e.g., in Table 5, pages 33 - 34; in Table 4; and in the synthetic sequence shown on page 32.

Conjugation of neurotrophins via thiolated lysine epsilon amino groups is shown, among other places, in Table 4.

The specific neurotrophins NGF, BDNF, NT-3, NT-4, and NT-6 are disclosed, e.g., at page 4, lines 15 - 18; page 10, lines 4 - 6; page 16, line 20 - page 17, line 40 (including Table 1); page 24, lines 15 - 16 and 28 - 29; and elsewhere.

The use of neurotrophin fragments in conjugates of the present invention is disclosed, *inter alia*, at page 4, lines 15 - 21, and elsewhere; the binding of NGF to trkA and

BDNF to trkB is disclosed, for example, in Table 1 (page 17); and the desirability of internalization of conjugates targeted to such neurotrophin receptors is disclosed, for example, at page 13, lines 28 - 32.

Respectfully submitted,

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